

#253 NetBioDyn, a smart Agent-Based software to intuitively model and simulate complex biological systems

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Modeling and teaching complex biological systems is a difficult process. The Multi-Agent paradigm has proved to be an appropriate approach, both in research and education, to grasp the complexity of these systems and investigating the underlying concepts of emergence and self-organization. As such, Agent-Based software are more and more used in life sciences to implement these models in virtual environments and simulate them. However, most of these software require knowledge and skills in programming languages, such as Java or the NetLogo environment. The gap between most of Agent-Based software prerequisites and the actual programming skills of (future) biologists has to be reduced and the processes of implementing a model and simulate it made more intuitive.

To answer this issue, we propose a smart, intuitive and open-source software aimed at biologists (students, teachers, researchers) to easily build and simulate complex biological mechanisms observed in multicellular and molecular systems. Thanks to its specific graphical user interface guided by the Multi-Agent paradigm (entities, behaviors and interactions) NetBioDyn does not need any prerequisite or knowledge in computer programming. It thus allows users to create in a simple way bottom-up models where unexpected behaviors can emerge from simple reactive interacting entities, and test hypothesis by creating various simulations, while providing at any time a simplified and complete view of the system's state. NetBioDyn has been successfully used to investigate systems such as two marine bacteria involved in a predator-prey relationship or the blood coagulation mechanisms in a small section of a vein. Moreover, NetBioDyn tackles the well-known problem of calibrating a model with interdependent, interconnected parameters by including a self-adjusting Multi-Agent System. This tools aims to automatically find the proper values for all the parameters involved in a simulation (interactions' probabilities, entities' lifespan etc.) according to real results obtained for example in vitro.

NetBioDyn, a smart Agent-Based software to intuitively model and simulate complex biological systems

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Objectives

To facilitate the process of **investigating, teaching and learning** complex biological systems

- **Creating realistic models and simulations** of complex biological systems to **investigate their dynamics and grasp complexity**
- **Reducing the gap** between the actual **programming skills** of (future) biologists and most modelling software needs
- Stimulating students **creativity** by promoting **abduction** (observe, build and test hypothesis)

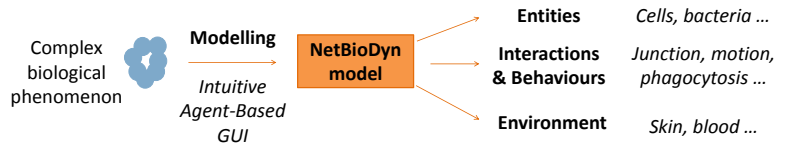
Proposal

To design an **intuitive Agent-Based software** aimed at biologists (students, teachers, researchers) to easily build and simulate complex biological mechanisms observed in **multicellular and molecular systems**

Modelling and teaching complex biological systems Scientific approach

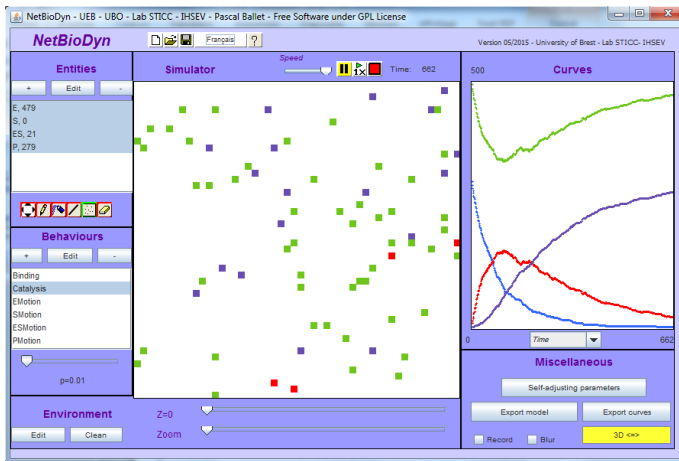
Using an **Agent-Based (discrete) approach** (vs. continuous)

- Focus on individuals (cells, molecules), their behaviour and their interactions, instead of population
 - Definition of **local interactions** leading to **global emerging behaviours**
 - **Variability** in cell population, cell differentiation
 - **Easier** to understand, do not require advanced mathematical skills
 - Model's **parameters are closer** to the field of biology
- Design of an **intuitive graphical user interface (GUI)** guided by the Multi-Agent paradigm



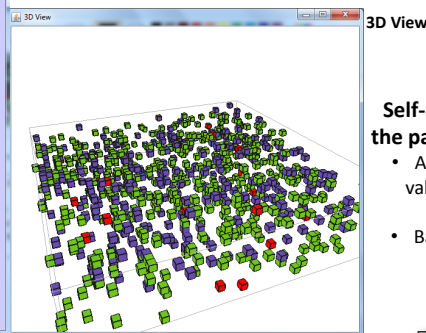
NetBioDyn, an intuitive and open-source software

<http://virtulab.univ-brest.fr/>



Specific graphical user interface

- Guided by the Multi-Agent paradigm (entities, behaviours and environment)
- No need of any prerequisite or knowledge in computer programming
- Providing at any time a simplified and complete view of the system's state (suitable *external representation*)



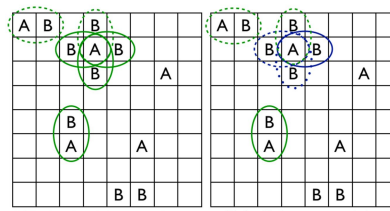
Self-adjusting mechanisms to calibrate the parameters of the model (test phase)

- Aiming at automatically find the proper values for all the parameters involved in a simulation
- Based on real results provided by users, obtained for example *in vitro*.

Enzyme kinetics
 $E + S \rightarrow ES \rightarrow P$

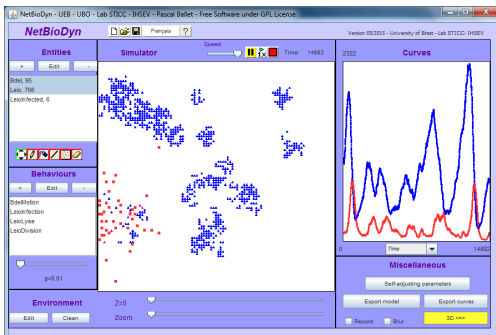
The environment is a 2D or 3D grid where entities interact according to their behaviours

- An entity occupies a whole grid cell
- Von Neumann neighbourhood: 4 neighbours in 2D and 6 in 3D
- Behaviours involving current entities are probabilistically performed at each time step



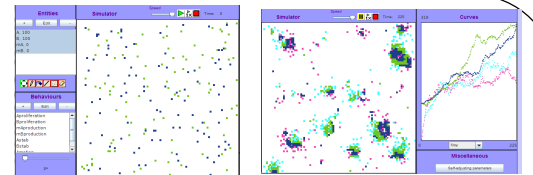
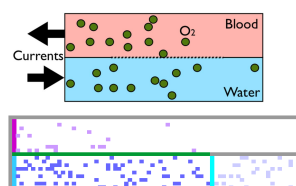
Name	behaviour	
Description	Short text of explanation	
Probability	Decimal number in [0, 1]	
Reactives	Positions	Products
A	+	A'
B	⊙ ↑ ← A → ↓ ⊗	B'
C	↑ ← A → ↓	C'

Examples of applications



Water-blood O₂ exchanges in Zebra Fishes

- Investigating the efficiency of the Zebra Fish counter-current respiratory system by **changing easily** the flow direction



A simple autopoietic system

- 4 entities: A, B and mA and mB (produced by A and B)
- A and B entities use each other's products (mA and mB) to multiply
- The system **converges** towards a balanced state

A predator-prey relationship involving two marine bacteria (*Bdellovibrio* and *Photobacterium leiognathi*)

- **Emergence** of interdependences and cycles between the two populations observed in real predator-prey systems

More examples of applications, tutorials and the software sources are available at <http://virtulab.univ-brest.fr/>